Remarks

The Office Action mailed August 8, 2006 has been carefully reviewed and the foregoing amendment has been made in consequence thereof.

Claims 1-17, 21-24, 26, and 32-48 are now pending in this application. Claims 1-5, 7-9, 16, 17, 37, and 40 stand rejected. Claims 3, 6-9, 37 and 40 stand objected to. Claims 6, 10-15, 21-24, 26, 32-36, 38, 39, and 41-48 have been withdrawn.

In accordance with 37 C.F.R. 1.136(a), a three month extension of time is submitted herewith to extend the due date of the response to the Office Action dated August 8, 2006, for the above-identified patent application from November 8, 2006, through and including February 8, 2007. In accordance with 37 C.F.R. 1.17(a)(3), authorization to charge a deposit account in the amount of $510.00 to cover this extension of time request also is submitted herewith.

Reconsideration of the election/restriction requirement imposed under 35 U.S.C. § 121 is respectfully requested.

Applicants note that Claims 6, 10-15, 21-24, 26, 32-36, 38, 39, and 41-48 have been withdrawn for being drawn to non-elected inventions. Applicants submit that the sequence ID numbers disclosed in the pending application are all clearly related and a search of one sequence ID number would be relevant to the other disclosed sequence ID numbers. Accordingly, Applicants respectfully request prosecution of Claims 6, 10-15, 21-24, 26, 32-36, 38, 39, and 41-48.

The objection to Claims 3, 6-9, and 40 due to an informality is respectfully traversed. Claims 3, 6-9, and 40 have been amended to address the issues raised in the Office Action. Accordingly, Applicants respectfully request that the objection to Claims 3, 6-9, and 40 be withdrawn.

The objection to Claims 37 and 40 due to an informality is respectfully traversed. Claims 37 and 40 have been amended to address the issues raised in the Office Action.

Accordingly, for at least the reasons set forth above, Applicants respectfully request that the objection to Claims 37 and 40 be withdrawn.

The first rejection of Claims 1-5 and 16-17 under 35 U.S.C. § 112, second paragraph, is respectfully traversed. Claim 1 has been amended to address the issues raised in the Office Action. Accordingly, for at least the reasons set forth above, Applicants respectfully request that the Section 112 rejection to Claims 1-5 and 16-17 be withdrawn.

The second rejection of Claims 1-5 and 16-17 under 35 U.S.C. § 112, second paragraph, is respectfully traversed. Applicants respectfully submit that one of ordinary skill in the art would recognize that phospholipase A2γ polypeptide clearly refers to a distinct polypeptide belonging to a family of calcium independent phospholipase A2. Specifically, paragraph [0005] of the specification recites "phospholipases A2 are a broad family of enzymes with varying kinetic and physical properties, and distinct functions." Accordingly, for at least the reasons set forth above, Applicants respectfully request that the Section 112 rejection to Claims 1-5 and 16-17 be withdrawn.

The first rejection of Claims 7 and 8 under 35 U.S.C. § 112, second paragraph, is respectfully traversed. Claim 7 has been amended to address the issues raised in the Office Action. Accordingly, for at least the reasons set forth above, Applicants respectfully request that the Section 112 rejection to Claims 7 and 8 be withdrawn.

The second rejection of Claims 7 and 8 under 35 U.S.C. § 112, second paragraph, is respectfully traversed. Applicants, submit that one reasonably skilled in the art would clearly understand the limitation "modulates enzymatic activity". Specifically, "modulates enzymatic activity" refers to a regulation of enzymatic activity that would be reasonably understood by one of skill in the art. Accordingly, for at least the reasons set forth above, Applicants respectfully request that the Section 112 rejection to Claims 7 and 8 be withdrawn.

The first rejection of Claims 16 and 17 under 35 U.S.C. § 112, second paragraph, is respectfully traversed. Claim 16 has been amended to address the issues raised in the Office

Action. Accordingly, for at least the reasons set forth above, Applicants respectfully request that the Section 112 rejection to Claims 16 and 17 be withdrawn.

The second rejection of Claims 16 and 17 under 35 U.S.C. § 112, second paragraph, is respectfully traversed. Claim 16 has been amended to address the issues raised in the Office Action. Accordingly, for at least the reasons set forth above, Applicants respectfully request that the Section 112 rejection to Claims 16 and 17 be withdrawn.

The rejection of Claim 17 under 35 U.S.C. § 112, second paragraph, is respectfully traversed. Claim 17 has been amended to address the issues raised in the Office Action. Accordingly, for at least the reasons set forth above, Applicants respectfully request that the Section 112 rejection to Claim 17 be withdrawn.

The first rejection of Claim 40 under 35 U.S.C. § 112, second paragraph, is respectfully traversed. Claim 40 has been amended to address the issues raised in the Office Action. Accordingly, for at least the reasons set forth above, Applicants respectfully request that the Section 112 rejection to Claim 40 be withdrawn.

The second rejection of Claim 40 under 35 U.S.C. § 112, second paragraph, is respectfully traversed. Claim 40 has been amended to address the issues raised in the Office Action. Accordingly, for at least the reasons set forth above, Applicants respectfully request that the Section 112 rejection to Claim 40 be withdrawn.

The rejection of Claims 1, 2, 4-5, 16, 17, and 40 under 35 U.S.C. § 112, first paragraph, is respectfully traversed. Applicants have amended the specification to include any isolated nucleic acid including a polynucleotide encoding a phospholipase A2γ and an in vitro expression construct in which any truncated iPLA2γ of any length is cloned downstream from a SV 40 promoter of a vector pEF. Specifically, newly added paragraph [00231] recites:

> In the exemplary embodiment, an isolated nucleic acid molecule is provided, wherein the isolated nucleic acid molecule includes a polynucleotide encoding a phospholipase A2γ polypeptide. In one embodiment, the phospholipase A2γ polypeptide catalyzes cleavage of fatty acids from the sn-2-position of phospholipids. In another embodiment, a vector

> including the nucleic acid molecule is provided. In an alternative embodiment a cell transformed or transfected with the vector is provided. In a further embodiment, a vector including the nucleic acid molecule is suitable for generating a transgenic mouse wherein a reporter gene encodes an enzyme capable of being detected by a colorimetric, fluorometric or luminometric assay. In one embodiment, the reporter gene encodes a luciferase.

Moreover, paragraph [00068], as filed, recites:

> Figure 29 shows expression of truncated iPLA$_2\gamma$ forms in an in vitro expression system. Truncated iPLA$_2\gamma$ constructs in vector pEF were expressed using a TnT® Quick Coupled Transcription Translation System and analyzed by SDS PAGE. The TnT® Quick Coupled Transcription/Translation Systems are single-tube, coupled transcription/translation reactions for eukaryotic in vitro translation. 88kDa, 77kDa, 74kDa, 70kDa, and 63kDa truncated forms are represented as 88, 77, 74, 70, and 63. Molecular weight standards are shown on the left and the predicted corresponding sizes of each of the iPLA2γ isoforms synthesized from alternative initiator methionines are indicated on the right.

Applicants submit that the amended paragraphs of the specification were clearly recited in the Claims. Because the Claims make-up a portion of the specification, Applicants submit that no new matter has been added. As such, Applicants submit that previously existing paragraph [00068] in combination with newly added paragraph [00231] would reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Accordingly, for at least the reasons given above, Applicants respectfully request that the Section 112 rejection of Claims 1, 2, 4-5, 16, 17, and 40 be withdrawn.

The rejection of Claims 7 and 9 under 35 U.S.C. § 112, first paragraph, is respectfully traversed. Applicants have amended the specification to include an isolated nucleic acid including a polynucleotide having at least about 90% indentity to sequence ID number 6, wherein the protein has or modulates PLA2γ and an antisense sequence that specifically hybridizes to sequence ID number 6. Specifically, newly added paragraph [00232] recites:

> Moreover, in one embodiment, an isolated nucleic acid including a polynucleotide having at least about 90% sequence identity with SEQ ID NO: 6 is provided. In one embodiment the isolated nucleic acid is encoded polypeptide that has or

> modulates enzymatic activity. In another embodiment, the isolated nucleic acid includes SEQ ID NO: 6.

Moreover, paragraph [00080], as filed, recites:

> Figure 25 reveals the high degree of N-terminal similarity of iPLA$_2\gamma$ from these three species. Within the first 210 amino acids, 145 amino acids are precisely conserved (69%). Comparing the full-length mouse iPLA$_2\gamma$ sequence (GenBank® accession number NP_080440), there is 82% identity of amino acid sequences when compared with the human sequence (SEQ ID NO: 1). If conservation of amino acid type is included, the homology rises to 90%. The differences in the sequences represent species differences. Nonetheless, all three sequences are clearly iPLA$_2\gamma$ and likely have the same or very similar functional attributes. In contrast, a similar comparison reveals only 38% homology of mouse NP_080440 to human iPLA$_2\beta$.

Applicants submit that the amended paragraphs of the specification were clearly recited in the Claims. Because the Claims make-up a portion of the specification, Applicants submit that no new matter has been added. As such, Applicants submit that previously existing paragraph [00080] in combination with newly added paragraph [00232] would reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Accordingly, for at least the reasons given above, Applicants respectfully request that the Section 112 rejection of Claims 7 and 9 be withdrawn.

The rejection of Claims 1, 2, 4, 5, 7, 9, 16, 17, and 40 under 35 U.S.C. § 112, first paragraph, is respectfully traversed. Applicants have amended the specification to enable a polynucleotide encoding any phospholipase A2γ, a ploynucleotide encoding a phospholipase A2γ, wherein the isolated polynucleotide sequence has at least a 90% sequence indentity to sequence ID number 6, a polynucleotide including any fragment length of sequence ID number 6 that encodes a polypeptide with phospholipase A2γ activity or is capable of modulating any undefined enzymic activity or fragement which will specifically hybridize to a polypeptide, vector, or host cell, and a method of making the poypeptide. Specifically, newly added paragraphs [00231], [00232], and [00233] recite:

> In the exemplary embodiment, an isolated nucleic acid molecule is provided, wherein the isolated nucleic acid molecule includes a polynucleotide encoding a phospholipase A2γ polypeptide. In one embodiment, the phospholipase A2γ

polypeptide catalyzes cleavage of fatty acids from the sn-2-position of phospholipids. In another embodiment, a vector including the nucleic acid molecule is provided. In an alternative embodiment a cell transformed or transfected with the vector is provided. In a further embodiment, a vector including the nucleic acid molecule is suitable for generating a transgenic mouse wherein a reporter gene encodes an enzyme capable of being detected by a colorimetric, fluorometric or luminometric assay. In one embodiment, the reporter gene encodes a luciferase.

Moreover, in one embodiment, an isolated nucleic acid including a polynucleotide having at least about 90% sequence identity with SEQ ID NO: 6 is provided. In one embodiment the isolated nucleic acid is encoded polypeptide that has or modulates enzymatic activity. In another embodiment, the isolated nucleic acid includes SEQ ID NO: 6.

Further, in one embodiment, an antisense sequence which specifically hybridizes to SEQ ID NO: 6 is provided. In another embodiment, an in vitro expression construct is provided in which a truncated $iPLA_2$ sequence is cloned downstream from the SV40 promoter of Invitrogen.

Moreover, paragraphs [00068] and [00080], as filed, recite:

Figure 29 shows expression of truncated $iPLA_2\gamma$ forms in an in vitro expression system. Truncated $iPLA_2\gamma$ constructs in vector pEF were expressed using a TnT® Quick Coupled Transcription Translation System and analyzed by SDS PAGE. The TnT® Quick Coupled Transcription/Translation Systems are single-tube, coupled transcription/translation reactions for eukaryotic in vitro translation. 88kDa, 77kDa, 74kDa, 70kDa, and 63kDa truncated forms are represented as 88, 77, 74, 70, and 63. Molecular weight standards are shown on the left and the predicted corresponding sizes of each of the iPLA2γ isoforms synthesized from alternative initiator methionines are indicated on the right.

Figure 25 reveals the high degree of N-terminal similarity of $iPLA_2\gamma$ from these three species. Within the first 210 amino acids, 145 amino acids are precisely conserved (69%). Comparing the full-length mouse $iPLA_2\gamma$ sequence (GenBank® accession number NP_080440), there is 82% identity of amino acid sequences when compared with the human sequence (SEQ ID NO: 1). If conservation of amino acid type is included, the homology rises to 90%. The differences in the sequences represent species differences. Nonetheless, all three sequences are clearly $iPLA_2\gamma$ and likely have the same or very similar functional attributes. In contrast, a similar comparison reveals only 38% homology of mouse NP_080440 to human $iPLA_2\beta$.

Applicants submit that the amended paragraphs of the specification were clearly recited in the Claims. Because the Claims make-up a portion of the specification, Applicants submit that no new matter has been added. As such, Applicants submit that previously existing paragraphs [00068] and [00080] in combination with newly added paragraphs [00231], [00232], and [00233] would reasonably enable one skilled in the art to make and use the claimed invention. Accordingly, for at least the reasons given above, Applicants respectfully request that the Section 112 rejection of Claims 1, 2, 4, 5, 7, 9, 16, 17, and 40 be withdrawn.

The rejection of Claim 5 under 35 U.S.C. § 112, first paragraph, is respectfully traversed. Applicants have amended the specification to enable a transgenic multi-cellular organism and host cells within a multi-cellular organism that have been transformed with a synthetic nucleic acid. Specifically, newly added paragraph [00231] recites:

> In the exemplary embodiment, an isolated nucleic acid molecule is provided, wherein the isolated nucleic acid molecule includes a polynucleotide encoding a phospholipase A2γ polypeptide. In one embodiment, the phospholipase A2γ polypeptide catalyzes cleavage of fatty acids from the sn-2-position of phospholipids. In another embodiment, a vector including the nucleic acid molecule is provided. In an alternative embodiment a cell transformed or transfected with the vector is provided. In a further embodiment, a vector including the nucleic acid molecule is suitable for generating a transgenic mouse wherein a reporter gene encodes an enzyme capable of being detected by a colorimetric, fluorometric or luminometric assay. In one embodiment, the reporter gene encodes a luciferase.

Moreover, paragraph [00137], as filed, recites:

> More specifically, to generate and purify the anti-iPLA$_2$γ peptide polyclonal antibodies used in the work described herein, New Zealand white rabbits were immunized with the iPLA$_2$γ synthetic peptide CENIPLDESRNEKLDQ (SEQ ID NO:26). This peptide (G3, 4 mg), dissolved in minimal volume of dimethylsulfoxide, was conjugated to maleimide-activated keyhole limpet hemocyanin (KILH, 2 mg) in 200 1d of 83 mM sodium phosphate, 0.9 M NaCl , and 0.1 mM EDTA at 22°C for two hours. After extensive dialysis against 83 mM sodium phosphate containing 0.9 mM NaCl, a 1:1 emulsion was made with the peptide-KLH conjugate and Freund's complete adjuvant. This emulsion was then injected subcutaneously into two anaesthetized New Zealand white rabbits. Two booster injections of a 1:1 emulsion of the peptide-KLH conjugate and

> Freund's incomplete adjuvant were given two and four weeks after the initial immunization. Serum was then collected for purification of the anti iPLA2γ antibodies.

Applicants submit that the amended paragraphs of the specification were clearly recited in the Claims. Because the Claims make-up a portion of the specification, Applicants submit that no new matter has been added. As such, Applicants submit that previously existing paragraph [00137] in combination with newly added paragraph [00231] would reasonably enable one skilled in the art to make and use the claimed invention. Accordingly, for at least the reasons given above, Applicants respectfully request that the Section 112 rejection of Claim 5 be withdrawn.

The rejection of Claims 1-5, 7, 9, and 40 under 35 U.S.C. § 102(a) as being anticipated by Tanaka et al. (Biochem. Biophysical Res. Commun., 2000, Vol. 272: 320-326, published June 07, 2000) (hereinafter referred to as "Tanaka") is respectfully traversed.

Tanaka describes an intercellular membrane-bound calcium-independent phospholipase A2. Specifically, Tanaka describes an independent phospholipase A2 that predominately exists in a membrane fraction and exhibits a phospholipase A2 activity in a calcium-independent manner when expressed in COS-7 cells. The transcript of the membrane-bound iPLA2 gene is ubiquitously observed as a single band of approximately 3.3 kb on Northern blot, with the most abundant expression in the skeletal muscle and heart. Notably, Tanaka does not describe nor suggest an isolated nucleic molecule configured to generate transgenically generated phospholipase A2 (TGiPLA$_2$) mice.

Claim 1 recites "an isolated nucleic acid molecule comprising a polynucleotide encoding a phospholipase A2γ polypeptide and configured to generate transgenically generated phospholipase A2 (TGiPLA$_2$) mice."

Tanaka does not describe nor suggest an isolated nucleic acid molecule as recited in Claim 1. More specifically, Tanaka does not describe nor suggest an isolated nucleic acid molecule configured to generate transgenically generated phospholipase A2 (TGiPLA$_2$) mice. Rather, in contrast to the recitations of Claim 1, Tanaka merely describes calcium-

independent phospholipase A2 that exhibits phospholipase A2 activity when expressed in COS-7 cells.

Accordingly, for at least the reasons set forth above, Claim 1 is submitted to be patentable over Tanaka.

Claims 2-5 depend from independent Claim 1. When the recitations of Claims 2-5 are considered in combination with the recitations of Claim 1, Applicants submit that dependent Claims 2-5 likewise are patentable over Tanaka.

Claim 7 recites "an isolated nucleic acid comprising a polynucleotide having at least about 90% sequence identity with SEQ ID NO: 6 wherein the encoded polypeptide has or modulates enzymatic activity, and wherein the isolated nucleic acid is configured to generate transgenically generated phospholipase A2 ($TGiPLA_2$) mice."

Tanaka does not describe nor suggest an isolated nucleic acid as recited in Claim 7. More specifically, Tanaka does not describe nor suggest an isolated nucleic acid configured to generate transgenically generated phospholipase A2 ($TGiPLA_2$) mice. Rather, in contrast to the recitations of Claim 7, Tanaka merely describes calcium-independent phospholipase A2 that exhibits phospholipase A2 activity when expressed in COS-7 cells.

Accordingly, for at least the reasons set forth above, Claim 7 is submitted to be patentable over Tanaka.

Claim 9 recites "an antisense sequence which specifically hybridizes to SEQ ID NO: 6, wherein the antisense is configured to generate transgenically generated phospholipase A2 ($TGiPLA_2$) mice."

Tanaka does not describe nor suggest an antisense sequence as recited in Claim 9. More specifically, Tanaka does not describe nor suggest an antisense sequence configured to generate transgenically generated phospholipase A2 ($TGiPLA_2$) mice. Rather, in contrast to the recitations of Claim 9, Tanaka merely describes calcium-independent phospholipase A2 that exhibits phospholipase A2 activity when expressed in COS-7 cells.

Accordingly, for at least the reasons set forth above, Claim 9 is submitted to be patentable over Tanaka.

Claim 40 recites "an in vitro expression construct in which a truncated $iPLA_2$ sequence is cloned downstream from the SV40 promoter of Invitrogen, wherein the in vitro expression construct is configured to generate transgenically generated phospholipase A2 ($TGiPLA_2$) mice."

Tanaka does not describe nor suggest an in vitro expression construct as recited in Claim 40. More specifically, Tanaka does not describe nor suggest an in vitro expression construct configured to generate transgenically generated phospholipase A2 ($TGiPLA_2$) mice. Rather, in contrast to the recitations of Claim 40, Tanaka merely describes calcium-independent phospholipase A2 that exhibits phospholipase A2 activity when expressed in COS-7 cells.

Accordingly, for at least the reasons set forth above, Claim 40 is submitted to be patentable over Tanaka.

For the reasons set forth above, Applicants respectfully request that the Section 102 rejection of Claims 1-5, 7, 9, and 40 be withdrawn.

The rejection of Claims 1-5, 7, 9, and 40 under 35 U.S.C. § 102(a) as being anticipated by Mancuso et al. (BJC., 2000, Vol. 275 (14): 9937-9945, published April 07, 2000) (hereinafter referred to as "Mancuso") is respectfully traversed.

Mancuso describes the identification of a complete organization of a putative phospholipase A2 through analysis of previously published expressed sequence tags, PCR of human heart cDNA, and 5'-rapid amplification of cDNA ends. A polymerase chain reaction and Northern blotting demonstrated a 3.4-kilobase message, which encoded a polypeptide with a maximum calculated molecular weight of 88476.9. The 3.4 kilobase message was present in multiple human parenchymal tissues including the heart, skeletal muscle, placenta, brain, liver, and pancreas. Notably, Mancuso does not describe nor suggest an isolated

nucleic molecule configured to generate transgenically generated phospholipase A2 ($TGiPLA_2$) mice.

Claim 1 is recited above.

Mancuso does not describe nor suggest an isolated nucleic acid molecule as recited in Claim 1. More specifically, Mancuso does not describe nor suggest an isolated nucleic acid molecule configured to generate transgenically generated phospholipase A2 ($TGiPLA_2$) mice. Rather, in contrast to the recitations of Claim 1, Mancuso describes identification of a complete organization of a putative phospholipase A2, wherein the phospholipase A2 demonstrates a 3.4-kilobase message.

Accordingly, for at least the reasons set forth above, Claim 1 is submitted to be patentable over Mancuso.

Claims 2-5 depend from independent Claim 1. When the recitations of Claims 2-5 are considered in combination with the recitations of Claim 1, Applicants submit that dependent Claims 2-5 likewise are patentable over Mancuso.

Claim 7 is recited above.

Mancuso does not describe nor suggest an isolated nucleic acid as recited in Claim 7. More specifically, Mancuso does not describe nor suggest an isolated nucleic acid configured to generate transgenically generated phospholipase A2 ($TGiPLA_2$) mice. Rather, in contrast to the recitations of Claim 7, Mancuso describes identification of a complete organization of a putative phospholipase A2, wherein the phospholipase A2 demonstrates a 3.4-kilobase message.

Accordingly, for at least the reasons set forth above, Claim 7 is submitted to be patentable over Mancuso.

Claim 9 is recited above.

Mancuso does not describe nor suggest an antisense sequence as recited in Claim 9. More specifically, Mancuso does not describe nor suggest an antisense sequence configured to generate transgenically generated phospholipase A2 (TGiPLA$_2$) mice. Rather, in contrast to the recitations of Claim 9, Mancuso describes identification of a complete organization of a putative phospholipase A2, wherein the phospholipase A2 demonstrates a 3.4-kilobase message.

Accordingly, for at least the reasons set forth above, Claim 9 is submitted to be patentable over Mancuso.

Claim 40 is recited above.

Mancuso does not describe nor suggest an in vitro expression construct as recited in Claim 40. More specifically, Mancuso does not describe nor suggest an in vitro expression construct configured to generate transgenically generated phospholipase A2 (TGiPLA$_2$) mice. Rather, in contrast to the recitations of Claim 40, Mancuso describes identification of a complete organization of a putative phospholipase A2, wherein the phospholipase A2 demonstrates a 3.4-kilobase message.

Accordingly, for at least the reasons set forth above, Claim 40 is submitted to be patentable over Mancuso.

For the reasons set forth above, Applicants respectfully request that the Section 102 rejection of Claims 1-5, 7, 9, and 40 be withdrawn.

The rejection of Claim 9 under 35 U.S.C. § 102(e) as being anticipated by Tang et al. (U.S. Patent 6,569,662) (hereinafter referred to as "Tang") is respectfully traversed.

Tang describes polynucleotides and proteins encoded by such polynucleotide. Specifically, the polynucleotides are isolated DNA sequences based on a secretory leader sequences. More specifically, the polynucleotides are assembled from expressed sequence tags that are isolated by sequencing by hybridization. Notably, Tang does not describe nor

suggest an isolated nucleic molecule configured to generate transgenically generated phospholipase A2 (TGiPLA$_2$) mice.

Claim 9 is recited above.

Tang does not describe nor suggest an antisense sequence as recited in Claim 9. More specifically, Tang does not describe nor suggest an antisense sequence configured to generate transgenically generated phospholipase A2 (TGiPLA$_2$) mice. Rather, in contrast to the recitations of Claim 9, Tang merely describes polynucleotides that are sequenced by hybridization.

Accordingly, for at least the reasons set forth above, Claim 9 is submitted to be patentable over Tang.

For the reasons set forth above, Applicants respectfully request that the Section 102 rejection of Claim 9 be withdrawn.

The rejection of Claim 9 under 35 U.S.C. § 102(e) as being anticipated by Yue et al. (U.S. Patent Application Publication 2004/0248243) (hereinafter referred to as "Yue") is respectfully traversed.

Yue describes human lipid metabolism enzymes (LME) and polynucleotides that identify and encode LME. Yue also describes expression vectors, host cells, antibodies, agonists, and antagonists that include the human lipid metabolism enzymes. Further, Yue describes methods for diagnosing, treating, and preventing disorders associated with the aberrant expression of LME. Notably, Yue does not describe nor suggest an isolated nucleic molecule configured to generate transgenically generated phospholipase A2 (TGiPLA$_2$) mice.

Claim 9 is recited above.

Yue does not describe nor suggest an antisense sequence as recited in Claim 9. More specifically, Yue does not describe nor suggest an antisense sequence configured to generate

transgenically generated phospholipase A2 (TGiPLA$_2$) mice. Rather, in contrast to the recitations of Claim 9, Yue describes human lipid metabolism enzymes (LME) and polynucleotides that identify and encode LME.

Accordingly, for at least the reasons set forth above, Claim 9 is submitted to be patentable over Yue.

For the reasons set forth above, Applicants respectfully request that the Section 102 rejection of Claim 9 be withdrawn.

The rejection of Claims 1-5, 7-9, 16, 17, 37, and 40 under 35 U.S.C. § 103(a) as being unpatentable over Tanaka or Mancuso and further in view of McTiernan et al. (U.S. Patent 5,917,123) (hereinafter referred to as "McTiernan") is respectfully traversed.

Tanaka and Mancuso are described hereinabove.

McTiernan describes transgenic nonhuman mammals that exhibit elevated levels of tumor necrosis factor alpha (TNFα) in myocardium relative to nontransgenic control mammals. McTiernan also describes a method for making transgenic TNFα non-human mammals for use in studying the treatment and prevention of cardiac dysfunction. Notably, McTiernan does not describe nor suggest an isolated nucleic molecule configured to generate transgenically generated phospholipase A2 (TGiPLA$_2$) mice. Rather, McTiernan describes a method of generating TNFα mammals.

Claim 1 is recited above.

None of Tanaka, Mancuso, or McTiernan, considered alone or in combination, describe or suggest an isolated nucleic acid molecule as recited in Claim 1. More specifically, none of Tanaka, Mancuso, or McTiernan, considered alone or in combination, describe nor suggest an isolated nucleic acid molecule configured to generate transgenically generated phospholipase A2 (TGiPLA$_2$) mice. Rather, in contrast to the recitations of Claim 1, Tanaka merely describes calcium-independent phospholipase A2 that exhibits phospholipase A2 activity when expressed in COS-7 cells, Mancuso describes identification

of a complete organization of a putative phospholipase A2, wherein the phospholipase A2 demonstrates a 3.4-kilobase message, and McTiernan describes a method of generating TNFα mammals. Applicants submit that merely reciting calcium independent phospholipase A2 and reciting a transgenic mammal does not make obvious a transgenically generated phospholipase A2 ($TGiPLA_2$) mouse. Specifcally, none of Tanaka, Mancuso, or McTiernan teach using calcium independent phospholipase A2 to trangenically generate a phospholipase A2 ($TGiPLA_2$) mouse.

Accordingly, for at least the reasons set forth above, Claim 1 is submitted to be patentable over Tanaka or Mancuso in view of McTiernan.

Claims 2-5, 16, and 17 depend from independent Claim 1. When the recitations of Claims 2-5, 16, and 17 are considered in combination with the recitations of Claim 1, Applicants submit that dependent Claims 2-5, 16, and 17 likewise are patentable over Tanaka or Mancuso in view of McTiernan.

Claim 7 is recited above.

None of Tanaka, Mancuso, or McTiernan, considered alone or in combination, describe or suggest an isolated nucleic acid as recited in Claim 7. More specifically, none of Tanaka, Mancuso, or McTiernan, considered alone or in combination, describe nor suggest an isolated nucleic acid configured to generate transgenically generated phospholipase A2 ($TGiPLA_2$) mice. Rather, in contrast to the recitations of Claim 7, Tanaka merely describes calcium-independent phospholipase A2 that exhibits phospholipase A2 activity when expressed in COS-7 cells, Mancuso describes identification of a complete organization of a putative phospholipase A2, wherein the phospholipase A2 demonstrates a 3.4-kilobase message, and McTiernan describes a method of generating TNFα mammals. Applicants submit that merely reciting calcium independent phospholipase A2 and reciting a transgenic mammal does not make obvious a transgenically generated phospholipase A2 ($TGiPLA_2$) mouse. Specifcally, none of Tanaka, Mancuso, or McTiernan teach using calcium

independent phospholipase A2 to trangenically generate a phospholipase A2 ($TGiPLA_2$) mouse.

Accordingly, for at least the reasons set forth above, Claim 7 is submitted to be patentable over Tanaka or Mancuso in view of McTiernan.

Claim 9 is recited above.

None of Tanaka, Mancuso, or McTiernan, considered alone or in combination, describe or suggest an antisense sequence as recited in Claim 9. More specifically, none of Tanaka, Mancuso, or McTiernan, considered alone or in combination, describe nor suggest an antisense sequence configured to generate transgenically generated phospholipase A2 ($TGiPLA_2$) mice. Rather, in contrast to the recitations of Claim 9, Tanaka merely describes calcium-independent phospholipase A2 that exhibits phospholipase A2 activity when expressed in COS-7 cells, Mancuso describes identification of a complete organization of a putative phospholipase A2, wherein the phospholipase A2 demonstrates a 3.4-kilobase message, and McTiernan describes a method of generating TNFα mammals. Applicants submit that merely reciting calcium independent phospholipase A2 and reciting a transgenic mammal does not make obvious a transgenically generated phospholipase A2 ($TGiPLA_2$) mouse. Specifcally, none of Tanaka, Mancuso, or McTiernan teach using calcium independent phospholipase A2 to trangenically generate a phospholipase A2 ($TGiPLA_2$) mouse.

Accordingly, for at least the reasons set forth above, Claim 9 is submitted to be patentable over Tanaka or Mancuso in view of McTiernan.

Claim 37 recites "a transgenic construct containing a promoter upstream of the full-length phospholipase A2 ($iPLA_2$) coding sequence (SEQ ID NO: 6) for myocardial specific expression of recombinant $iPLA_2$ in transgenically generated phospholipase A2 ($TGiPLA_2$) mice."

None of Tanaka, Mancuso, or McTiernan, considered alone or in combination, describe or suggest a transgenic construct as recited in Claim 37. More specifically, none of Tanaka, Mancuso, or McTiernan, considered alone or in combination, describe nor suggest a transgenic construct for myocardial specific expression of recombinant $iPLA_2$ in transgenically generated phospholipase A2 ($TGiPLA_2$) mice. Rather, in contrast to the recitations of Claim 37, Tanaka merely describes calcium-independent phospholipase A2 that exhibits phospholipase A2 activity when expressed in COS-7 cells, Mancuso describes identification of a complete organization of a putative phospholipase A2, wherein the phospholipase A2 demonstrates a 3.4-kilobase message, and McTiernan describes a method of generating TNFα mammals. Applicants submit that merely reciting calcium independent phospholipase A2 and reciting a transgenic mammal does not make obvious a transgenically generated phospholipase A2 ($TGiPLA_2$) mouse. Specifcally, none of Tanaka, Mancuso, or McTiernan teach using calcium independent phospholipase A2 to trangenically generate a phospholipase A2 ($TGiPLA_2$) mouse.

Accordingly, for at least the reasons set forth above, Claim 37 is submitted to be patentable over Tanaka or Mancuso in view of McTiernan.

Claim 40 is recited above.

None of Tanaka, Mancuso, or McTiernan, considered alone or in combination, describe or suggest an in vitro expression construct as recited in Claim 40. More specifically, none of Tanaka, Mancuso, or McTiernan, considered alone or in combination, describe nor suggest an in vitro expression construct configured to generate transgenically generated phospholipase A2 ($TGiPLA_2$) mice. Rather, in contrast to the recitations of Claim 40, Tanaka merely describes calcium-independent phospholipase A2 that exhibits phospholipase A2 activity when expressed in COS-7 cells, Mancuso describes identification of a complete organization of a putative phospholipase A2, wherein the phospholipase A2 demonstrates a 3.4-kilobase message, and McTiernan describes a method of generating TNFα mammals. Applicants submit that merely reciting calcium independent phospholipase A2 and reciting a transgenic mammal does not make obvious a transgenically generated phospholipase A2

(TGiPLA$_2$) mouse. Specifcally, none of Tanaka, Mancuso, or McTiernan teach using calcium independent phospholipase A2 to trangenically generate a phospholipase A2 (TGiPLA$_2$) mouse.

Accordingly, for at least the reasons set forth above, Claim 40 is submitted to be patentable over Tanaka or Mancuso in view of McTiernan.

For the reasons set forth above, Applicants respectfully request that the Section 103 rejection of Claims 1-5, 7-9, 16, 17, 37, and 40 be withdrawn.

Moreover, Applicants respectfully submit that the Section 103 rejection of the presently pending claims is not a proper rejection. As is well established, obviousness cannot be established by combining the teachings of the cited art to produce the claimed invention, absent some teaching, suggestion, or incentive supporting the combination. None of Tanaka, Mancuso, or McTiernan, considered alone or in combination, describe or suggest the claimed combination. Furthermore, in contrast to the assertion within the Office Action, Applicants respectfully submit that it would not be obvious to one skilled in the art to combine any of Tanaka, Mancuso, and McTiernan because there is no motivation to combine the references suggested in the art. Additionally, the Examiner has not pointed to any prior art that teaches or suggests to combine the disclosures, other than Applicants' own teaching.

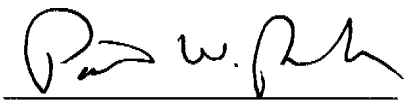
As the Federal Circuit has recognized, obviousness is not established merely by combining references having different individual elements of pending claims. Ex parte Levengood, 28 U.S.P.Q.2d 1300 (Bd. Pat. App. & Inter. 1993). MPEP 2143.01. Rather, there must be some suggestion, outside of Applicants' disclosure, in the prior art to combine such references, and a reasonable expectation of success must be both found in the prior art, and not based on Applicant's disclosure. In re Vaeck, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). In the present case, neither a suggestion or motivation to combine the prior art disclosures, nor any reasonable expectation of success has been shown.

Furthermore, it is impermissible to use the claimed invention as an instruction manual or "template" to piece together the teachings of the cited art so that the claimed invention is

rendered obvious. Specifically, one cannot use hindsight reconstruction to pick and choose among isolated disclosures in the art to deprecate the claimed invention. Further, it is impermissible to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art. The present Section 103 rejection is based on a combination of teachings selected in an attempt to arrive at the claimed invention. Since there is no teaching nor suggestion in the cited art for the combination, the Section 103 rejection appears to be based on a hindsight reconstruction in which isolated disclosures have been picked and chosen in an attempt to deprecate the present invention. Of course, such a combination is impermissible, and for these reasons, along with the reasons given above, Applicants request that the Section 103 rejection of Claims 1-5, 7-9, 16, 17, 37, and 40 be withdrawn.

In view of the foregoing amendments and remarks, all the claims now active in this application are believed to be in condition for allowance. Reconsideration and favorable action is respectfully solicited.

Respectfully Submitted,



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